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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/624,946	07/25/00	GREENE M	PENN-0708

EXAMINER	
TUNG, T	
ART UNIT	**PAPER NUMBER**
1656	6

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DATE MAILED: 07/05/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/624,946	Greene et al.
Examiner	**Art Unit**
Joyce Tung	1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above, claim(s) 1-4 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 5-11 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1656.

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-4, drawn to a method of detecting molecules expressing a selected epitope in a sample, classified in class 435, subclass 7.1.

   II. Claims 5-11, drawn to a system and kit of detecting molecules expressing a selected epitope in a sample, classified in class 422/435, subclass 61/287.2.

2. The inventions are distinct, each from the other because of the following reasons: Inventions I and II are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case, the process of claims 1-4 can be practiced by hand, while the system of claims 5-11 can be used to practice another and materially different process, for example, to detect nucleic acid.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Ms. Kathleen A. Tyrell on 6/26/2001 a provisional election was made with traverse to prosecute the invention of II, claims -11. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-4 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

6. The title of the invention is not descriptive because the old title is directed to a rapid, sensitive and quantitative method for immuno-detection of epitopes on molecules using a single chain Fv for the epitope of a constrained epitope specific CDR while the claim language is direct a system for detecting molecules expressing a selected epitope. A new title is required that is clearly indicative of the invention to which the claims are directed.

Information Disclosure Statement

7. The references AB and AH lined through in PTO-1449 filed 3/12/2001 were not in the Application and the reference AB even does not have publication date. All references in PTO-1449 are required to have publication date

Claim Rejections - 35 U.S.C. § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 5-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 5-11 are vague and indefinite because it is unclear whether or not the molecules expressing a selected epitope are cells. In Example 1, there are cells expressing epitope (See pg. 15, lines 20-34). It is suggested to clarify uncertainty.

b. Claims 5-11 are vague and indefinite because it is unclear what is meant by the language "a single chain Fv". It appears that variable domain of antibody has light chain and heavy chain. Thus it is unclear what is meant by the language. It is suggested to clarify uncertainty.

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5-6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (Jpn. J. Cancer Res., 1985, Vol. 86, pg. 885-889) in view of Skerra et al. (Science, 1988, Vol. 240, pg. 1038-1041).

Suzuki et al. disclose a method of detecting antigens in sera. The method involves using a first monoclonal antibodies to bind the circulating antigens is immobilized. A second monoclonal antibody biotinylated binds to the antigen (See pg. 885, the Abstract). Suzuki et al. also indicates that there is a very sensitive antigen detection system has been developed (See pg.

885 column 1, first paragraph) and the method of Suzuki et al. has a 10^3-fold higher sensitivity (See pg. 885, column 2, first paragraph).

Since the claim language of claim 5 is confusing as indicated in section 8(a) above, the claim language is interpreted as detecting a molecule which is an epitope. Thus the teaching of Suzuki et al. suggest the limitations in claims 5-6 and 8-11 because the epitope is a protein which has specific site to bind to an antibody and the antigen of Suzuke et al. acts as an epitope, the first antibody acts as the epitope anchor for immobilizing the molecule to the surface as recited in claim 6. The second antibody act as the epitope detector which binds to oligonucleotide as recited in claim 5(b) since the oligonucleotide amplified generates signal from Southern blot hybridization. Since the language "a single chain Fv for the selected epitope" is unclear as set forth in section 5(b), it is interpreted as a regular Fv fragment which binds to antigen. Antibody has Fv fragment which binds to antigen and this was well known in the art.

Suzuki et al. do not disclose using the epitope detector comprising complementarity determining region.

Skerra et al. disclose an expression system producing a completely function antigen-binding fragment of antibody in *E. coli* containing complementarity-determining regions (CDR) per chain that determine the specificity for antigen recognition (See pg. ~~240~~ 1038, column 1, first paragraph and the Abstract).

The teachings of Suzuki et al. and Skerra et al. suggest the limitations of claims 5-6 and 8-11. Claims 5-6 and 8-11 are drawn to a system and kit of detecting a molecule expressing a selected epitope comprising a selected surface on which the epitope binds and an epitope detector comprising a single chain Fv or CDR.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the teachings of Suzuki et al., and Skerra et al. to make the system as claimed with a reasonable expectation of success because the system of Suzuki et al. has a 10^3-fold higher sensitivity (See pg. 885, column 2, first paragraph) and detect antigen in sera at a level below the detection limit of traditional ELISA method (See pg. 885, the Abstract), the method of Skerra et al. produce a completely functional antigen-binding fragment of an antibody comprising CDR. Although none of the references above discloses a kit used for performing the detection, one of ordinary skill in the at the time of the instant invention would have packed all components needed for the system as claimed because this is routine practice in the art at the time of the instant invention. It would have been prima facie obvious to make the system and kit as claimed.

11. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Suzuki et al. (Jpn. J. Cancer Res., 1985, Vol. 86, pg. 885-889) in view of Skerra et al. (Science, 1988, Vol. 240, pg. 1038-1041) as applied to claims 5-6 and 8-11 above, and further in view of Quentin-Millet et al. (4,965,205).

The teachings of Suzuki et al. and Skerra et al. are set forth in section 10 and Suzuki et al. and Skerra et al. do not disclose using the epitope detector comprising hemagglutinin or polyhistidine as a universal epitope detector.

Quentin-Millet et al. disclose using ELISA involving anti- filamentous hemagglutinin antibody to estimate the amount toxin antigen (See column 4, lines 26-30). The method of Quentin-Millet et al. produced a high yield toxin antigen which is detected by using ELISA involving anti- filamentous hemagglutinin antibody.

The teachings of Suzuki et al. and Skerra et al. and Quentin-Millet et al. suggest the limitations of claim 7 which recites further limitation to claim 5 in which the epitope detector comprises hemagglutinin or polyhistidine as a universal epitope detector.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the teachings of Suzuki et al., Skerra et al. and Quentin-Millet et al. to make the system as claimed with a reasonable expectation of success because the system of Suzuki et al. has a 10^3-fold higher sensitivity (See pg. 885, column 2, first paragraph) and detect antigen in sera at a level below the detection limit of traditional ELISA method (See pg. 885, the Abstract), the method of Skerra et al. produce a completely functional antigen-binding fragment of an antibody containing CDR and anti- hemagglutinin antibody has been used for detection in ELISA as taught by Quentin-Millet et al. It would have been prima facie obvious to make the system and kit as claimed.

12. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1656 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

June 30, 2001